Remarks

Claims 1, 4, 19 and 23 have been amended to specifically define the "5 or 6 membered heterocyclic ring" and the "8-10 membered bicyclic heteroaryl" which are "X" in the formula "$(CH_2)_q$-X" for R^1 , R^2 , R^3 , R^4 and $R.^5$

The amendments to claim 1 also specifically define the mono- and bi-cyclic heteroaryl groups which are "A."

Claims 3 and 19 have been amended to delete compounds where "B" is naphthyl.

Rejection Under 35 USC§112, first paragraph

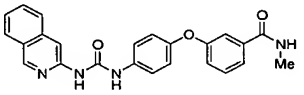
After the amendments herein, all claims now specifically identify the 5 and 6 membered heterocyclic rings and the mono- and bi-cyclic heteroaryl groups that define the compounds of formula I. Applicants clearly provide sufficient guidance to make and use the compounds now defined in the claims of this application. The synthesis of the compounds is described generally on pages 22-26 and in the examples. Methods for preparing pharmaceutical compositions with these compounds and methods for administering compounds in the treatment of patients are provided on pages 27-38. Dosages are provided on page 41. To the extent the disclosure does not provide specific dosages, it would at most involve routine experimentation, if any at all, for one skilled in the art to treat any one of the recited diseases with the compounds of this invention. Furthermore, it would not be undue experimentation to test these compounds for the activity disclosed in the specification. Such testing is routine, performed on a day to day basis by those skilled in the art . No evidence has been presented to suggest that the claimed compounds can not be synthesized or that they would not be active or that they could not be used without undue experimentation, as is required to maintain a viable rejection under 35 USC §112, first paragraph, see In re Marzocchi, 439, F. 2d 220, 169 USPQ 367 (CCPA 1971).

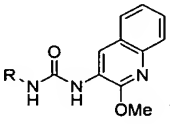
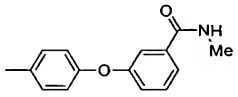
In view of the above, Applicants traverse the rejection of claims 1-7, 19-25 and 29-30, under 35 USC §112, first paragraph. This rejection is based on the

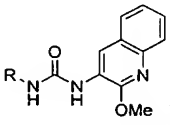
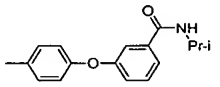
allegation that the specification does not provide an enabling disclosure for using all of the compounds of claim 1.

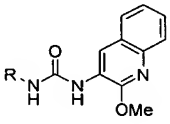
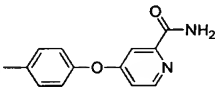
Applicants maintain the express disclosure within the specification enables the full scope of the pending claims as set forth above . Applicants also maintain these claims are further supported and enabled by the specification in view the state of the art and the disclosures incorporated by reference in the specification.

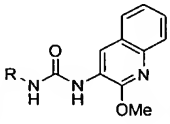
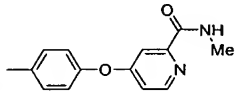
Raf active aryl and hetaryl ureas were known to those skilled in the art prior to this invention. For example, WO-02/062763 and WO 02/085857 disclose how to make and use urea compounds which inhibit raf kinase wherein the moiety "A" is a bi-cyclic heteroaryl group, more specifically a quinolinyl or isoquinolinyl group. The compounds of examples 104-112 of WO-02/062763 are illustrated below:

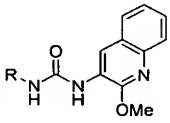
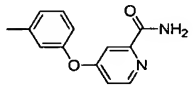
Compound 104 

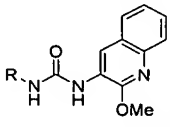
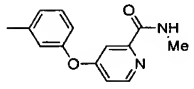
Compound 105  where R is 

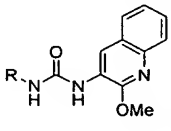
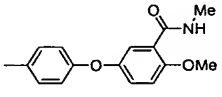
Compound 106  where R is 

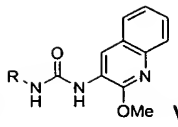
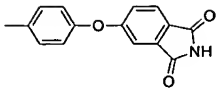
Compound 107  where R is 

Compound 108  where R is 

Compound 109  where R is 

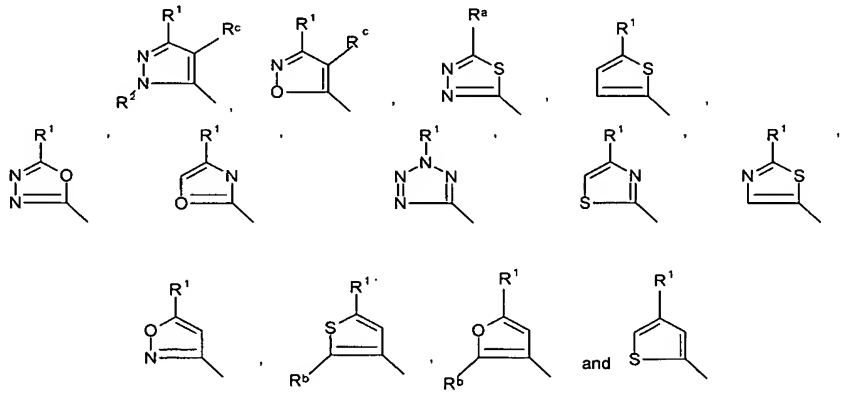
Compound 110  where R is 

Compound 111  where R is 

Compound 112  where R is 

WO 02/085857 provides 8 examples of ureas which inhibit raf kinase and have the moiety "A" as a quinolinyl or isoquinolinyl group. These published applications are mentioned on page 25 of the specification and are incorporated by reference in the subject application (see page 73, last line). These disclosures coupled with the express disclosure in the subject application (examples of the bi-cyclic heteroaryl groups quinolinyl and indazol in Examples 4, 7, 15 and 20) clearly enable the bi-cyclic heteroaryl hetaryl ureas claimed herein such as where 'A" is indazole, quinoline, quinazoline, imidazopyrimidine or naphtyridine. No evidence has been presented to the contrary.

The published applications WO 99/32106 and WO 99/32455 disclose how to make and use a large number of mono-cyclic heteroaryl ureas which inhibit raf kinase. For example, on page 7 of WO 99/32106, the heteraryl moiety A is said to be preferably selected from the group consisting of:



Over 300 compounds are exemplified in this publication alone. Additional pyrazoles which inhibit raf kinase are disclosed in WO 99/32455. These applications are also mentioned on page 25 of the specification and are incorporated by reference. Based on these disclosures, the specification is clearly enabling with respect to making and

using hetaryl ureas of formula I herein where "A" is pyrrole, furan, thiophene, imidazole, pyrazole, thiazole, oxazole, isoxazole, isothiazole, triazole, tetrazole, thiadiazole, oxadiazole, pyridine, pyrimidine, pyridazine, pyrazine or triazine.

As to whether compounds where B of formula I is pyridyl or naphthyl are enabled, reference is made to the published application WO 99/32106, discussed above. This publication provides over 30 hetaryl urea compounds where the moiety "B" is pyridyl. The broad generic teachings on page 46 and 47 of this publication also show how to prepare starting materials that will provide a pyridine for moiety "B" of a hetaryl urea. WO 00 42012, another published application mentioned on page 25 of the subject application and incorporated by reference, discloses an aryl urea compound in entry 9 where moiety "B" is pyridyl. Based on these disclosures and the express teachings within the subject application, one skilled in the art could make and use the compounds of this invention where the moieties "A," "L", "M" and "Q" of formula I are as defined in the claims. No evidence has been presented to the contrary.

Published prior art application WO 01/36403, discloses methods for preparing aryl and hetaryl ureas where "B" is naphthyl. More specifically, examples 6-9 show how to prepare naphthylamine starting materials and example 10 shows how to prepare ureas from these starting materials. With this knowledge, one skilled in the art could clearly apply the teachings of the subject application to prepare and use of compounds of formula I where "B" is naphthyl, without undue experimentation.

As to whether the specification is enabling for compounds wherein L is not -O-. Applicants submit one skilled in the art would recognize how to incorporate all groups defined by "L" without undue experimentation. The published application WO 99/32106 discloses hetaryl urea compounds where the moiety "L" can be -O-, -O-CH_2-, -CH_2-, -C_2H_4-, -C(O)- , -NH- , -N(Me)- ,-N(Et)-, -NH-C(O)-, -C(O)NH-, -S-, -SCH_2-, -CH_2S-, -CH(OH)-, or a single bond. The compounds of these examples have values for "L" which are consistent with the values (a)–(h) recited in the claims herein and each has been shown to inhibit raf kinase. With such information known in the art (and incorporated by reference), the subject specification clearly enables those compounds wherein "L" is other than –O-.

For the reasons indicated above, and the fact that the Patent and Trademark Office has not provided any evidence shedding doubt that the invention can not be made and used as stated, Applicants maintain that they have provided more than adequate guidance to enable the claimed invention and submit all claims meet the requirements of 35 U.S.C. §112, first and second paragraphs.

The Commissioner is hereby authorized to charge any fees associated with this response or credit any overpayment to Deposit Account No. 13-3402.

Respectfully submitted,

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